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EDITORIAL

Guest Editorial

Choriocarcinoma and Related Trophoblastic Tumors in Women

OUR OBSERVATIONS OVER the past 12 years have led to the concept that the gestational trophoblastic disease constitutes a continuous biological spectrum which may present itself morphologically as hydatidiform mole, invasive mole (chorioadenoma destruens) or choriocarcinoma. The histological criteria for delineating these entities are sufficiently specific to permit morphological classification when adequate tissue is carefully studied.^{1,2,3} However, numerous cases are readily misdiagnosed even by expert observers. Our data show that such purely morphological considerations have little bearing on the final response to appropriately applied chemotherapy.^{4,5,6,7}

The most definitive criterion for the evaluation of chemotherapy is the behavior of the urinary chorionic gonadotropin titre. Accordingly, great emphasis is placed on the careful collection and refrigeration of complete 24-hour urine specimens and upon meticulous care in the concentration and bioassay of these specimens. To date, we have

found no bioassay system superior to the mouse-uterine-weight method for the detection of minimal traces of residual disease. Other bioassay or immunoassay systems such as those currently used for the diagnosis of pregnancy are not sufficiently sensitive for this purpose. Some laboratories have found that exquisitely sensitive radio-immunoassay methods applied to serum are suitable for monitoring chemotherapy. Not enough time has elapsed to permit definitive correlation between such radio-immunoassay results and the clinical course of disease through several years of follow-up. Nevertheless, it appears highly probable that radio-immunoassay may soon be able to replace bioassay for such critical determinations.

The duration of the disease process and the associated extent of disease before therapy are decisive factors in determining the results of chemotherapy. In patients with metastatic disease whose course is less than four months in duration before chemotherapy is begun and whose initial urinary titre is less than 100,000 I.U. per 24 hours, we may expect a 95 percent complete remission rate.^{5,7} In patients with a longer history and with higher initial titres the complete remission rate falls to 36 percent. The necessity for early diagnosis and prompt treatment can not be overemphasized.

An extension of this principle is also demonstrated by the almost uniform eradication of early non-metastatic trophoblastic disease by primary chemotherapy in place of hysterectomy, thus preserving reproductive function for these women.^{6,8}

The severe toxicity imposed by intensive, intermittent regimens of Methotrexate or actomyocin

D will prove entirely reversible in patients whose renal, hepatic and hemopoietic functions are shown to be normal before therapy, provided such patients are given the benefit of adequate laboratory and clinical surveillance during and after treatment.^{5,7,9,10}

The endocrinological study of patients with trophoblastic disease indicates that some tumors produce a thyreotropic substance, thus inducing a hyperthyroid state in the host which responds to specific onclytic therapy.^{11,12}

Patients with trophoblastic disease differ endocrinologically from normally pregnant women in failing to exhibit increasing levels of urinary estrogen excretion. They also exhibit much lower levels of serum placental lactogen in proportion to the gonadotropin titre than one observes in normal pregnancy.¹³ These biochemical differences may not only provide a practical basis for differential diagnosis but also lead to further comprehension of the nature of the metabolic derangements occurring in neoplastic trophoblast. Such analyses will be greatly facilitated by the ready availability for basic study of human choriocarcinoma maintained as heterologous transplants in the untreated hamster's cheek-pouch. More recently such tissue has been maintained in the brain of untreated monkeys as well as in tissue culture.^{14,15,16}

The practical as well as the fundamental advances in the area of trophoblastic tumors during the past decade has been both gratifying and exhilarating. Nevertheless, there remain major challenges for further study especially with respect to etiology, pathogenesis, epidemiology and treatment.

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A Sequence of Change

IT IS INCUMBENT upon us to continue to examine the profound changes which are occurring in attitudes toward health and well-being, and as a profession we must do our best to prepare ourselves for what is likely to be a new order of things. There seems to be a certain sequence which is worth noting in many of these changes. Passive acceptance, or even indifference, gives way to a more positive emphasis on equality, conformity and acceptable standards, which in turn gives way to a more activist, at times militant, emphasis on individual fulfillment and self-realization, even to the point of non-conformity. This sequence may be seen in attitudes of people toward themselves, toward others, toward health and toward health care.

People are viewing themselves and their lot in life with changing attitudes. Gradually yesteryear's more or less passive acceptance of one's place in the social or economic scale was almost wholly displaced by the idea that one man is as good as another, and now this notion of equality among men is already being eroded by an increasing emphasis on individuality and the right to personal expression and fulfillment. In their attitudes toward others who are less fortunate, people are replacing indifference, neglect or even repression with individual and group voluntary efforts, and even massive governmental programs to help bring